

## CLAIMS

1. A method for determining the significance of a given nucleic acid polymorphism or mutation, in a nucleic acid molecule, on the structural properties of a protein encoded by said nucleic acid molecule comprising:

5 (a) exposing the protein encoded by said nucleic acid molecule to at least one protease; and

(b) determining whether, or to what extent, proteolytic cleavage takes place; and, optionally,

10 (c) comparing this proteolytic cleavage with that of the wild-type protein when exposed to the same protease(s).

2. A screening method for determining the significance of a plurality of variants of at least one gene comprising:

15 (a) obtaining a sample of protein encoded by each of said variants;

(b) exposing each protein to at least one protease;

(c) determining whether, or to what extent, proteolytic cleavage takes place; and

(d) comparing the proteolytic cleavage with that of the wild-type protein when exposed to the same protease(s).

20 3. A method according to claim 1 or 2 wherein said protein is exposed to a plurality of proteases.

4. A method according to claim 3 wherein at least some of said proteases and so attack different sites within the protein.

5. A method according to any preceding claim wherein said protease(s) comprises any one or more of the following: trypsin, chymotrypsin, proteinase K, aminopeptidase, carboxypeptidase, collagenase, elastase, Kallikrein, metalloendopeptidase, papain or pepsin.

10 6. A method according to any preceding claim wherein a plurality of proteins are exposed to said protease(s).

7. A method according to claims 3-6 wherein said proteins are exposed to said proteases, or vice versa, simultaneously.

15 8. A method according to any preceding claim wherein said protein(s) is exposed to said different proteases either simultaneously or successively.

20 9. A method according to any preceding claim wherein said protein(s) are exposed to said protease(s) under conditions that support the activity of said protease(s).

10. A method according to any preceding claim wherein digestion of said protein(s) is terminated by adding at least one protease inhibitor to the reaction.

11. A method according to any preceding claim wherein proteolytic cleavage is determined using a conventional protein assay.

5 12. A method according to claim 11 wherein said assay involves SDS-PAGE analysis.

13. A method according to claim 12 wherein said analysis is followed by staining or blotting.

10 14. A method according to any preceding claim wherein additional studies are undertaken to determine the functionality of the protein variant.

15 15. A method according to any preceding claim wherein part (a) involves further exposing the wild-type protein to said at least one protease and part (b) involves determining whether and to what extent proteolytic cleavage of said wild-type protein takes place.

20 16. A method according to any preceding claim wherein the wild-type protein and, optionally, the variant protein are subjected to the conditions of the proteolytic reaction, in the absence of the said protease(s), and then the extent of proteolytic cleavage is determined.